

## **REMARKS**

### **Amendments**

Claims 1, 3, 5, 7, 8 and 9 have been amended to delete the phrase “shown in” in favor of “consisting essentially of”. This amendment is intended to provide “closed claim language” to the polypeptides themselves and NOT to the claimed compositions of matter. That is, the polypeptides consist essentially of the sequence shown in SEQ ID NO:2. The claimed compositions of matter can therefore comprise elements other than the recited polypeptides. The deletion of “consisting essentially of” in favor of “comprising” in the claims is clearly not a narrowing amendment.

New claims 10-13 are added. These claims find support in the specification at, *inter alia*, Table 1.

### **Rejection of Claims 1-9 Under 35 U.S.C. §112, first paragraph**

Claims 1-9 stand rejected under 35 U.S.C. §112, first paragraph as allegedly lacking written description. Applicants respectfully traverse the rejection.

The Office Action asserts that the amino acid substitution variants of SEQ ID NO:2 lack written description. The Office Action states that there is no requirement that “one of skill in the art to find polypeptides that are amino acid substitution variants of SEQ ID NO:2 that specifically bind to an anti-Ehrlichia antibody” and appears to assert that the specific locations in which substitutions can be made must be disclosed. The Office Action also asserts that no structural description of the claimed variants is provided. This is not the standard for written description. The standard for written description does not state that one of skill in the art must be able to determine amino acid substitution variants of SEQ ID NO:2 without “looking” or

“hunting” for the variants. The written description requirement also does not require that the specific locations where amino acids can be substituted or the specific structure be disclosed.

Rather, the standard for written description requires that one of skill in the art must recognize that the applicant was in possession of the claimed genus, that is, variants of SEQ ID NO:2. Importantly:

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, ¶1, “Written Description” Requirement, 66 Fed. Reg. 1099, 1106 (2001) (citations omitted).

Satisfactory disclosure of a representative number of species depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. Description of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces. One species can adequately support a genus.

What is a representative number of species depends on whether one of skill in the art would recognize that the Applicants were in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed or claimed. Distinguishing characteristic such as:

- A. partial structure;
- B. physical and/or chemical properties;

- C. functional characteristics;
- D. known or disclosed correlation between structure and function;
- E. method of making; and
- F. combinations of A-E

should be considered. All of these factors, in view of the level of skill and knowledge in the art in light of and consistent with the written description, should be considered. See M.P.E.P. § 2163.

In the instant case, the partial structure of claimed variants are known, *i.e.*, sequences that having at least 85% identity to SEQ ID NO:2. Therefore, the variants have about 17 amino acids in common with the 20 amino acid long SEQ ID NO:2. The physical properties and functional characteristics of the variants are known. That is, the specification teaches that the variants specifically bind to an anti-*Ehrlichia* antibody and also teaches how to test if such variants specifically bind to an anti-*Ehrlichia* antibody. See specification page 10, line 6 through page 11, line 6; page 11, line 21- page 16, line 8; Example 1. Methods of making the variants of SEQ ID NO:2 are well-known in the art and are described in the specification. See *e.g.* page 5, lines 7-14; page 6, line 3 through page 7, line 5; page 7, line 12 through page 9, line 7; page 18, line 19 through page 19, line 13; page 7, line 6 through page 9, line 7. One of skill in the art could make and test variants of invention given the specification and the knowledge in the art.

Therefore, one of skill in the art would recognize that applicant was in possession of the necessary common attributes of features of the elements possessed by the members of the genus in view of the species disclosed because the partial structure, physical and/or chemical properties, functional characteristics, and methods of making the claimed variants is disclosed in

the specification. The written description does not have to be of such specificity that it would provide individual support for each species that the genus embraces.

The Office Action baldly asserts that it is not routine in the art to screen for multiple substitutions or multiple modifications of other types and positions within the polypeptide's sequence where modifications can be made with a reasonable expectation of success in obtaining similar activity are limited in any polypeptide and the result of such modifications is unpredictable. The Office cites no authority for this proposition and this is not the standard for written description. Nevertheless, while this may be true for large proteins with many modifications, the instant disclosure contemplates only about 3 amino acid substitutions in any claimed about 20 amino acid polypeptide and clearly states that the changes are phenotypically silent or conservative amino acid substitutions. Due to the small size of the claimed polypeptides, the fact that the variants have at least 85% identity to SEQ ID NO:2, and the fact that the variants specifically bind to anti-*Ehrlichia* antibody, one of skill in the art could make and test the variants without undue experimentation.

Finally, the Office Action concludes that the species specifically disclosed are not representative of the genus because the genus is highly variant. Applicants do not agree that the genus of claimed variants is highly variant. As stated above, the claimed variants are phenotypically silent amino acid variants and conservative amino acid variants that have at least 85% identity to SEQ ID NO:2, and specifically bind to an anti-*Ehrlichia* antibody. The genus is not highly variant.

Therefore, when all factors are considered, one of skill in the art would recognize from the disclosure that the Applicants were in possession of the claimed invention. Applicants respectfully request withdrawal of the rejection.

**Rejection of Claims 1-9 Under 35 U.S.C. §112, first paragraph**

Claims 1-9 stand rejected under 35 U.S.C. § 112, first paragraph as allegedly lacking enablement. Applicants respectfully traverse the rejection.

The Office Action asserts states that under the enablement requirement a structural description of the claimed variants must appear in the specification. The Office Action asks “How can one skilled in the art make and use the claimed composition of matter or article of manufacture comprising phenotypically silent amino acid substitution variants of SEQ ID NO:2 if there is no structural description associated with these substitution variants?”

The Office Action has completely disregarded the fact that there is indeed structural description of the claimed variants. The variants are phenotypically silent or conservative amino acid variant that have at least 85% identity to SEQ ID NO:2, and that specifically bind to anti-*Ehrlichia* antibody. The standard for enablement does not require that the specific amino acid sequence for each claimed variant be disclosed in the specification. Rather, the proper inquiry is whether one of skill in the art is able to make and use the claimed the variants, from the specification coupled with information known in the art, without undue experimentation.

One of skill in the art certainly could design, make, and test phenotypically silent and conservative amino acid variants of SEQ ID NO:2. It is routine to make amino acid substitutions of an about 20 amino acid polypeptide and to test the resulting variants for specific binding to an anti-*Ehrlichia* antibody. The test of enablement is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. " *In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (citing

*In re Angstadt*, 190 USPQ 214, 217-19 (CCPA 1976)); M.P.E.P. §2164.06. Time and expense are merely factors in this consideration and are not the controlling factors. *United States v. Telectronics Inc.*, 8 USPQ2d 1217, 1223 (Fed. Cir. 1988).

The specification teaches that making and testing the polypeptides and variants of the invention are trivial as outlined in the specification at, *inter alia*, page 10, line 6 through page 11, line 6; page 11, line 21 through page 16, line 8; Example 1, page 17, line 11 through page 19, line 13. Thus, it is trivial and routine to screen for the substitutions possible while maintaining 85% or greater identity to SEQ ID NO:2 and while maintaining binding to anti-*Ehrlichia* antibodies, according to the specification. One of skill in the art would expect to identify the claimed variants using only routine experimentation.

Once the claimed variants are made, one of skill in the art can use them to, *inter alia*, detect the presence of anti-*Ehrlichia* antibodies.

The Office Action further asserts that it is not routine to screen multiple substitutions with a reasonable expectation of success in obtaining similar anti-*Ehrlichia* antibody binding. The Office Action asserts that the expectation in obtaining similar anti-*Ehrlichia* antibody binding is limited in any polypeptide and the result of such modifications is unpredictable. The Office Action asserts that one of skill in the art would not expect any tolerance to multiple substitutions. A reasonable expectation of success is not the standard for enablement. Applicants remind the Office that the standard for enablement is whether one reasonably skilled in the art (1) could make and use the invention (2) from the disclosures in the patent coupled with information known in the art (3) without undue experimentation. Additionally, the Office Action has provided no data or citation to support these bald assertions. Applicants have cited several authorities to demonstrate that amino acid substitutions can indeed be made to

polypeptides with a reasonable expectation of creating phenotypically silent or conservative amino acid variants. See Response to Office Action mailed August 29, 2003, page 6, last paragraph through page 8, last paragraph.

Finally, the Office Action states that there is no requirement that one of skill in the art to find polypeptides that are amino acid substitution variant of SEQ ID NO:2 that specifically bind to an anti-*Ehrlichia* antibody and asserts that specific locations in which substitutions can be made must be disclosed in the specification to meet the enablement requirement. This is not the standard for enablement. The standard for enablement does not state that one of skill in the art must be able to determine amino acid substitution variants of SEQ ID NO:2 without “looking” or “hunting” for the variants. The enablement requirement also does not require that the specific locations where amino acids can be substituted or the specific structure be disclosed as discussed above.

One of skill in the art could make and use the claimed variants in light of the specification and knowledge in the art, without undue experimentation. Applicants respectfully request withdrawal of the rejection.

#### **Rejection of Claims 1-9 Under 35 U.S.C. §102(b)**

Claims 1-9 stand rejected under 35 U.S.C. §102(b) as allegedly anticipated by Rikihisa *et al.* Applicants respectfully traverse the rejection.

Under 35 U.S.C. § 102, a claim is anticipated only if each and every element as set forth in the claim is found in a single art reference. *Verdegaal Bros. v. Union Oil Co.*, 2 USPQ2d 1051, 10533 (Fed. Cir. 1987); *In re Recombinant DNA Technology Patent and Contract Litigation*, 30 USPQ2d 1881, 1885 (S.D. Ind.1993) (“A patent is anticipated only if all the elements and limitations of the claims are found within a single, prior art reference.”); *Structural*

*Rubber Products Co. v. Park Rubber Co.*, 223 USPQ 1264, 1270 (Fed. Cir. 1984) (All elements of the claimed invention must be contained in a single prior art disclosure and must be arranged in the prior art disclosure as in the claimed invention); M.P.E.P. § 2131. Furthermore, no difference may exist between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of invention. *In re Recombinant DNA Technology Patent and Contract Litigation*, 30 USPQ2d 1881, 1885 (S.D. Ind.1993). Also, the identical invention must be described or shown in as complete detail as is contained in the claim. *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989); *Chester v. Miller*, 15 USPQ2d 1333 (Fed. Cir. 1990); M.P.E.P. § 2131.

The Office Action asserts that there is nothing on record to show that the claimed device differs from the device of Rikihisa. The Office Action asserts that Rikihisa teaches the use of a device comprising *Ehrlichia* antigen and that the applicant has provided no side-by-side comparison to show that the claimed polypeptides differ from the Rikihisa polypeptides. However, Rikihisa does not teach or suggest an element of the claims, that is, a polypeptide consisting essentially of SEQ ID NO:2 and amino acid substitution variants thereof. Therefore, Rikihisa cannot anticipate the claims. The Office Action appears to assert, however, that a teaching of polypeptides consisting essentially of SEQ ID NO:2 and substitution variants are inherently present in Rikihisa.

The fact that a certain characteristic may occur or be present in a prior art reference is not sufficient to establish the inherency of that characteristic. *In re Rijckaert*, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993); *In re Oelrich*, 666 F.2d 578, 581-82, 212 USPQ 323, 326 (CCPA 1981). "To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would

be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.' " *In re Robertson*, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999) (citations omitted); MPEP §2112.01. "In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." *Ex parte Levy*, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990) (emphasis in original); MPEP §2112.01.

The Office has not provided a basis in fact and/or technical reasoning to show that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art. Rikihisa does not teach or suggest the use of polypeptide fragments in devices and in particular does not teach or suggest the particular fragment shown in SEQ ID NO:2. Nor has that Office Action alleged that the whole recombinant protein antigens in Rikihisa would be fragmented in any way.

Additionally, the claimed compositions of matter provide greater sensitivity than the reagents taught in Rikihisa (*i.e.*, whole, recombinant proteins). See attached declaration of Dr. Chandrashekar, paragraphs 2-3 and 6-7. Therefore, the claimed compositions of matter differ from those of Rikihisa because they provide greater sensitivity than those described in Rikihisa.

Rikihisa does not anticipate claims 1-9 because Rikihisa does not teach, suggest, or inherently disclose each and every element of claims 1-9. Applicants respectfully request withdrawal of the rejection.

**Rejection of Claims 1-9 Under 35 U.S.C. §112, second paragraph**

Claims 1-9 stand rejected under 35 U.S.C. §112, second paragraph as allegedly lacking definiteness. Applicants respectfully traverse the rejection.

The Office Action asserts that claims 1-9 are indefinite for the use of the term “an isolated polypeptide shown in SEQ ID NO:2.” Claims 1, 3, 5, 7, 8, and 9 have been amended to recite “a polypeptide consisting essentially of SEQ ID NO:2.”

The Office Action asserts that claim 21 is indefinite because it recites “phenotypically silent amino acid substitution variants.” The test for definiteness is whether “those skilled in the art would understand what is claimed when the claim is read in light of the specification.” *Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 1 USPQ2d 1081, 1088 (Fed. Cir. 1986). One of skill in the art would understand the meaning of phenotypically silent amino acid substitution variants given the specification. The specification teaches phenotypically silent amino acid substitution variants and how to identify such variants at, *inter alia*, page 7, line 10 through page 9, line 7. In particular, the specification teaches that “guidance concerning how to make phenotypically silent amino acid substitutions is provided in Bowie *et al.*, *Science*, 247:1306-1310 (1990).” See specification, page 7, lines 14-17. One of skill in the art would understand the meaning of phenotypically silent amino acid substitution variants given the specification.

The Office Action asserts that claims 5 and 9 are indefinite because it is unclear if a product or process is being claimed. Claims 5 and 9 clearly recite that “the label indicates” a certain process. Thus, one of skill in the art would understand that claims 5 and 9 are further describing the label of the claimed compositions of matter. The claim is therefore definite and applicants respectfully request withdrawal of the rejection.

The Office Action asserts that claims 5 and 9 are indefinite for the use of the term “under conditions.” The claims recite that certain polypeptides that specifically bind to an anti-*Ehrlichia* antibody, are contacted with a test sample suspected of comprising antibodies to *Ehrlichia*, under conditions that allow polypeptide/antibody complexes to form. The claim is describing an extremely well known method of detecting the presence of antibodies to a bacterial pathogen comprising the detection of polypeptide/antibody complexes. One of skill in the art, given the specification, which includes working examples of such detection, would clearly understand the meaning of “under conditions” that allow polypeptide/antibody complexes to form because one of skill in the art would be very familiar with such methods. The claims are therefore definite and applicants respectfully request withdrawal of the rejection.

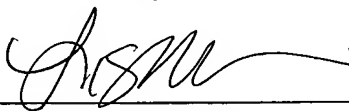
#### **Conclusion**

Applicants respectfully submit that the claims are in a condition for allowance. If the Examiner is of the opinion that that a telephone conference would expedite the prosecution of the application, the Examiner is encouraged to contact Applicants undersigned representative.

Respectfully submitted,

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by:



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